

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor: Meir Stern Confirmation No.: 1887
Application No.: 10/699,582 Patent No.: 7,335,377 B2
Filing Date: October 31, 2003 Patent Date: February 26, 2008
For: TRANSDERMAL DELIVERY SYSTEM FOR Attorney Docket No.: 85189-5300
DRIED PARTICULATE OR LYOPHILIZED
MEDICATIONS

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 C.F.R. § 1.322

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Patentees hereby respectfully request the issuance of a Certificate of Correction in connection with the above-identified patent. The corrections are listed on the attached Form PTO-1050. The corrections requested are as follows:

Column 30:

Line 39 (claim 12, line 2), before "carbohydrates," insert -- the group consisting of --.
Line 42 (claim 13, line 2), before "sucrose", insert -- the group consisting of --.
Line 55 (claim 17, line 3), before "an anti-oxidant," insert -- the group consisting of --.

Column 31:

Line 14 (claim 24, line 1), after "claim", delete "23" and insert -- 19 --.
Line 18 (claim 26, line 1), after "claim", delete "25" and insert -- 19 --.
Line 39 (claim 32, line 3), after "consisting of a backing layer," delete "and".

Column 32:

Line 10 (claim 42, line 2), before "carbohydrates," insert -- the group consisting of --.
Line 13 (claim 43, line 2), before "sucrose", insert -- the group consisting of --.
Line 27 (claim 47, line 3), before "an anti-oxidant," insert -- the group consisting of --.

The requested changes are to correct errors of a clerical or typographical nature and do not involve changes that would constitute new matter or require reexamination. Regarding claims 12, 13, 17, 43, 43 and 47, proper Markush language has been added, while for claims 24 and 26, the changes were made to provide proper antecedent basis.

A fee of \$100 is believed to be due for this request. Please charge the required fees to Winston & Strawn LLP Deposit Account No. 50-1814. Please issue a Certificate of Correction in due course.

Respectfully submitted,

6-16-08
Date


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212-294-3311

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,335,377 B2
APPLICATION NO. : 10/699,582
DATED: February 26, 2008
INVENTOR(S) : Stern et al.

Page 1 of 1

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 30:

Line 39 (claim 12, line 2), before "carbohydrates," insert -- the group consisting of --.
Line 42 (claim 13, line 2), before "sucrose", insert -- the group consisting of --.
Line 55 (claim 17, line 3), before "an anti-oxidant," insert -- the group consisting of --.

Column 31:

Line 14 (claim 24, line 1), after "claim", delete "23" and insert -- 19 --.
Line 18 (claim 26, line 1), after "claim", delete "25" and insert -- 19 --.
Line 39 (claim 32, line 3), after "consisting of a backing layer," delete "and".

Column 32:

Line 10 (claim 42, line 2), before "carbohydrates," insert -- the group consisting of --.
Line 13 (claim 43, line 2), before "sucrose", insert -- the group consisting of --.
Line 27 (claim 47, line 3), before "an anti-oxidant," insert -- the group consisting of --.

occluded and 0.5 for the adjacent non-occluded sites accounting for a minor response.

TABLE 5

	Draize Irritation Index	Grade
<u>Erythema and Eschar Formation</u>		
No erythema	0	
Very slight erythema (barely perceptible)	1	
Well defined erythema	2	
Moderate to severe erythema	3	
Severe erythema (beet redness) to eschar formation preventing grading of erythema	4	
Edema formation	—	
No edema	0	
Very slight edema (barely perceptible)	1	
Slight edema (edges of area well defined by definite raised border)	2	
Moderate edema (raised approximately 1 mm)	3	
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4	
Total possible score for irritation	8	

TABLE 6

	Cumulative Irritation Index	Mean Score
Response category		
Negligible	0 to 0.4	
Slight	0.5 to 1.9	
Moderate	2.0 to 4.9	
Severe	5.0 to 8.0	

b. Tolerability Evaluation

Pain scores were in the range of 0-50 mm. The pain score per subject was an average from 10 ViaDerm applications. The average values (per site of treatment) ranged from 2.1 mm to 7.02 mm. Those values are considered negligible.

The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying current knowledge, readily modify and/or adapt for various applications such specific embodiments without undue experimentation and without departing from the generic concept, and, therefore, such adaptations and modifications should and are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments. It is to be understood that the phraseology or terminology employed herein is for the purpose of description and not of limitation. The means, materials, and steps for carrying out various disclosed functions may take a variety of alternative forms without departing from the invention. Thus the expressions "means to . . ." and "means for . . .", or any method step language, as may be found in the specification above and/or in the claims below, followed by a functional statement, are intended to define and cover whatever structural, physical, chemical or electrical element or structure, or whatever method step, which may now or in the future exist which carries out the recited function, whether or not precisely equivalent to the embodiment or embodiments disclosed in the specification above, i.e., other means or steps for carrying out the same functions can be used; and it is intended that such expressions be given their broadest interpretation.

What is claimed is:

1. A printed patch for transdermal administration of at least one therapeutically active agent comprising a non-adhesive liner and a dried pharmaceutical composition that comprises the active agent or agents present on the non-adhesive liner, wherein the non-adhesive liner is made of a material that is not permeable to the active agent or agents.
2. The printed patch according to claim 1 wherein the patch further comprises at least one layer selected from the group consisting of a backing layer, an adhesive and a microporous liner layer.
3. The printed patch according to claim 1 wherein the dried pharmaceutical composition is hydrophilic.
4. The printed patch according to claim 3 wherein the dried pharmaceutical composition comprises at least one hydrophilic therapeutically active agent.
5. The printed patch according to claim 4 wherein the hydrophilic therapeutically active agent is selected from the group consisting of proteins, polypeptides, peptides, poly-nucleotides, oligonucleotides, growth factors, hormones, and salts thereof.
6. The printed patch according to claim 5 wherein the hydrophilic therapeutically active agent is human growth hormone.
7. The printed patch according to claim 5 wherein the hydrophilic therapeutically active agent is human insulin.
8. The printed patch according to claim 4 wherein the dried pharmaceutical composition further comprises at least one additional hydrophilic agent.
9. The printed patch according to claim 8 wherein the hydrophilic agent is mannitol.
10. The printed patch according to claim 8 wherein the dried pharmaceutical composition comprises human growth hormone and mannitol.
11. The printed patch according to claim 8 wherein the dried pharmaceutical composition further comprises a stabilizer.
12. The printed patch according to claim 11 wherein the stabilizer is selected from carbohydrates, amino acids, and polymers.
13. The printed patch according to claim 12 wherein the carbohydrate is a disaccharide selected from sucrose and trehalose.
14. The printed patch according to claim 11 wherein the dried pharmaceutical composition comprises human growth hormone, mannitol and trehalose.
15. The printed patch according to claim 11 wherein the dried pharmaceutical composition comprises human growth hormone, mannitol and trehalose.
16. The printed patch according to claim 1, which contains below 20% by weight of water and wherein the active agent remains stable for at least three months at about 22° C.
17. The printed patch according to claim 1 wherein the pharmaceutical composition further comprises at least one component selected from an anti-oxidant, a buffering agent and a preservative.
18. A method for transdermal administration of a dried pharmaceutical composition comprising at least one therapeutically active agent comprising:
 - (a) generating at least one micro-channel in an area of the skin of a subject, and
 - (b) affixing a printed patch according to claim 1 to the area of skin in which at least one micro-channel is present.
19. The method according to claim 18 which further comprises:
 - (c) achieving a therapeutic blood concentration of the active agent for a predetermined period of time.

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20. The method according to claim 18 wherein the dried pharmaceutical composition is hydrophilic.
21. The method according to claim 20 wherein the dried pharmaceutical composition comprises at least one hydrophilic therapeutically active agent.
22. The method according to claim 21 wherein the hydrophilic therapeutically active agent is selected from the group consisting of proteins, polypeptides, peptides, polynucleotides, oligonucleotides, growth factors, hormones, and salts thereof.
23. The method according to claim 22 wherein the hydrophilic therapeutically active agent is human growth hormone.
- 19 24. The method according to claim 23 wherein the predetermined period of time is about 1 to 6 hours.
25. The method according to claim 22 wherein the therapeutically hydrophilic active agent is human insulin.
- 19 26. The method according to claim 25 wherein the predetermined period of time is about 4 to 6 hours.
27. The method according to claim 18 wherein the patch comprises at least two electrodes integrated thereto.
28. The method according to claim 18 comprising inducing iontophoresis of the at least one therapeutically active agent into the skin of the subject.
29. The method according to claim 28 wherein inducing the iontophoresis comprises inducing the iontophoresis subsequent to the generating of the at least one micro-channel.
30. The printed patch according to claim 1 comprising at least two electrodes integrated thereto.
31. A system for transdermal delivery of an active therapeutic agent from a dried pharmaceutical composition comprising: an apparatus for facilitating transdermal delivery of an active therapeutic agent through skin of a subject, said apparatus capable of generating at least one micro-channel in an area on the skin of the subject, and the printed patch 35 according to claim 1.
32. The system according to claim 31 wherein the patch further comprises at least one layer selected from the group consisting of a backing layer, ~~and~~ an adhesive layer and a microporous liner layer.
33. The system according to claim 31 wherein the dried pharmaceutical composition is hydrophilic.
34. The system according to claim 33 wherein the dried pharmaceutical composition comprises at least one hydrophilic therapeutically active agent.
35. The system according to claim 34 wherein the hydrophilic therapeutically active agent is selected from the group consisting of proteins, polypeptides, peptides, polynucleotides, oligonucleotides, growth factors, hormones, and salts thereof.
36. The system according to claim 35 wherein the hydrophilic therapeutically active agent is human growth hormone.
37. The system according to claim 35 wherein the hydrophilic therapeutically active agent is human insulin.
38. The system according to claim 34 wherein the dried pharmaceutical composition further comprises at least one additional hydrophilic agent.

39. The system according to claim 38 wherein the hydrophilic agent is mannitol.

40. The system according to claim 38 wherein the dried pharmaceutical composition comprises human growth hormone and mannitol.

41. The system according to claim 38 wherein the dried pharmaceutical composition further comprises a stabilizer.

42. The system according to claim 41 wherein the stabilizer is selected from carbohydrates, amino acids and polymers.

43. The system according to claim 42 wherein the carbohydrate is a disaccharide selected from sucrose and trehalose.

44. The system according to claim 41 wherein the pharmaceutical composition comprises human growth hormone, mannitol and sucrose.

45. The system according to claim 41 wherein the pharmaceutical composition comprises human growth hormone, mannitol and trehalose.

46. The system according to claim 31 wherein the active agent remains stable for at least three months at about 22° C.

47. The system according to claim 31 wherein the pharmaceutical composition further comprises at least one component selected from an anti-oxidant, a buffering agent and a preservative.

48. The system according to claim 31 comprising an apparatus for facilitating transdermal delivery of a therapeutically active agent through skin of a subject, said apparatus comprising:

a. an electrode cartridge comprising at least one electrode; and

b. a main unit comprising a control unit which is adapted to apply electrical energy to the electrode when the electrode is in vicinity of the skin, typically generating current flow or one or more sparks, enabling to cause ablation of stratum corneum in an area beneath the electrode, thereby generating at least one micro-channel.

49. The system according to claim 48 wherein the electrode cartridge is removable.

45 50. The system according to claim 48 wherein the electrode cartridge comprises a plurality of electrodes capable of generating a plurality of micro-channels of uniform shape and dimensions.

51. The system according to claim 48 wherein the electrical energy is of radio frequency.

52. The system according to claim 31, wherein the printed patch comprises at least two electrodes.

53. The system according to claim 52, wherein the electrodes are adapted to induce iontophoresis of the at least one therapeutically active agent into the skin of the subject.

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